

♀ Genital System

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The Ovary

Formed of:

1 Germinal Epith:-

Simple cubical w gradually e' $\uparrow$ age change into s. sq.

The name is wrong as it does not give ova.

2 Tunica Albuginea = dense fibrous c.t. under the germinal epith.

3 - Outer cortex = Stroma + Ovarian follicles.

4 - Inner Medulla = highly vascular loose c.t.

Bl. vs. ns. & lymph vs. enter & leave at the ovarian hilum.

Cortical Stroma:

Spindle shaped fibroblast like cells on a background of collagen & reticul. fs.

Collagen fibres $\uparrow$ e' age (maximum at menopause). Stromal cellularity is hormone dependant.

Functions of stromal cells $\left\{ \begin{array}{l} \text{support developing ova.} \\ \text{give theca folliculi cells.} \\ \text{secrete } \text{♀} \text{ hrs. (estrogen \& androgen)} \end{array} \right.$

Ovarian Follicles

present in the cortex. 5 types:

1 Primordial Follicles:

- Just under tunica albuginea. Formed bet. 6th & 9th month of fetal life.

- Formed of 1- γ Oocyte (25 μ m) surrounded by 1 layer of Flat [follicular] cells

1- γ Oocyte: have large vesicular nucleus e' clear nucleolus, diploid N^o of chromosomes. Cytoplasm (Ooplasm) contains: mit., G.A., ER. & lysosomes.

2 Primary Follicles:

At puberty, primordial follicles $\xrightarrow{\text{FSH}}$ 1- γ follicles. 2 types:

(a) Unilaminar 1- γ Follicles:

- 1- γ Oocyte $\uparrow$ in size (40 μ m) in arrested prophase of 1st meiotic division
- Follicular cells become cuboidal.

(b) Multilaminar (preantral) 1- γ Follicle:

- 1- γ Oocyte reaches 50 μ m. ($\uparrow$ N^o of organelles)
- Follicular cells proliferate $\rightarrow$ many layers of polyhedral cells = granulosa cells
- a thick glycopn. memb. = Zona pellucida (rich in GAGs) forms bet. 1- γ Oocyte & granulosa cells (both share in its formation)
- stromal cells around the follicle form concentric layers $\rightarrow$ capsule [Theca folliculi]
- * follicles move deep in the cortex.

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[3] 2nd [Antral] Follicle :

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- liquor folliculi, secreted by granulosa cells accumulate bet. them. It contains GAGs + steroid binding ptns. The spaces containing liquor folliculi unite → 1 large cavity = **Antrum**.
- 1st Oocyte enlarge (120 μ m) & is pushed to one side.
- Theca folliculi differentiates into ┌ theca externa.
└ " interna

[4] 3rd Mature Graafian Follicle :

- Large 2 — 2.5 cm, occupies the whole thickness of cortex & bulges on the surface
- Formed of :
 - (a) 1st Oocyte: 150 μ m & just before ovulation changes into 2nd Oocyte (1n) = haploid no.
 - (b) **Zona pellucida**: thick glycoprotein memb. surrounding the oocyte.
 - (c) **Corona radiata**: granulosa cells around the oocyte (become columnar). Have cytoplasmic processes w/ penetrate Z. pellucida & contact microvilli projecting from the oocyte by gap junctions.
 - (d) **Cumulus Oophorus**: granulosa cells around the Corona radiata & separating the oocyte from follicular fluid.
 - (e) **Granulosa Cells**: 3 — 4 layers of polyhedral cells lining the follicular cavity & secrete follicular fluid & aromatase enz. that converts androgen coming from theca interna → Estrogen
 - (f) **Basement memb.** separating granulosa cells from Theca folliculi.
 - (g) **Theca Interna**: polyhedral cells enclosing fenestrated capillaries. They either directly secrete **estrogen** or secrete **androgen** by aromatase of granulosa cells → estrogen. By E/M. have features of steroid secreting cells [SER, many mit, fat droplets].
 - (h) **Theca Externa**: Compact layer of stromal (fibroblast-like) cells & no secretory function. No clear boundary bet. Th. externa & interna or surrounding stroma.

[5] Atretic Follicles :

- In each menstrual cycle, about 20 1st follicles are activated but only one reaches maturity liberating the Oocyte. the other follicles undergo atresia.
- Atresia occurs at any stage of the developing follicles [primordial, 1st, 2nd or 3rd follicles].
- The Oocyte dies & the surrounding cells degenerate.
- Macrophages phagocytose debris.

- Degenerating primordial or 1ry follicles completely resorb & leaves no scar, but 2ry & 3ry follicles leave a scar of collagen (stays for a long time)

Fate of M.G.F. [Ovulation]

- High estrogen level $\rightarrow$ surge of L.H. [at mid cycle = day 14] $\xrightarrow{\text{stim.}}$ Ovulation
- $\uparrow\uparrow$ pressure of follicular fluid $\rightarrow$ loosening of granulosa cells $\rightarrow$ rupture of MGF
- $\rightarrow$ liberation of oocyte into the peritoneal cavity. The oocyte is surrounded by Zona pellucida, corona radiata & cumulus Oophorus & picked up by F. tube. It remains viable for 24 hrs then undergo autolysis.
- Follicular fluid & some blood (from theca interna) are expelled into the peritoneal cavity (pain sensitive) $\rightarrow$ mid cycle pain.
 - the antrum contains bl. clot.
 - Granulosa cells & theca interna cells $\rightarrow$ Corpus luteum.

Corpus luteum

Temporary endocrine gland in the ovarian cortex. Results from ovulation & under effect of L.H. It produces high level of progesterone & moderate estrogen.

Formation & structure:

- Release of the follicular fluid $\rightarrow$ collapse of the follicle & the wall of the corpus luteum is folded. Blood in the cavity $\rightarrow$ bl. clot w is gradually removed. In animals, the central bl. clot is present $\rightarrow$ Corpus Hemorrhagicum.
- Granulosa cells: $\uparrow\uparrow$ in size, become rich in sER, mit., fat droplets & lipochrome pigment $\rightarrow$ Yellow color in fresh section & called. Granulosa lutein cells $\rightarrow$ progesterone.
- Theca Interna cells: show EM features of steroid secreting cells [but smaller than granulosa lutein cells, & fewer fat droplets] & called Theca lutein cells $\rightarrow$ estrogen.

Fate of Corpus luteum:

- If no pregnancy occurs, L.H $\downarrow$ & the corpus luteum [C.L. of Menstruation] degenerates within 10-12 days, degenerated cells are phagocytosed by macrophages. Fibroblasts invade it $\rightarrow$ dense fibrous c.t. $\rightarrow$ Corpus Albicans
- If pregnancy Occurs: trophoblast of the embryo secrete HCG [similar to LH] w stimulate growth of CL $\rightarrow$ [C.L. of Pregnancy] w secrete progesterone & estrogen until the placenta is formed. (4-5 months) then degenerates & replaced by Corpus albicans.

$\therefore$ Types of Corpora

1. Corpus luteum of menstruation.
2. " " " pregnancy.
3. Corpus haemorrhagicum
4. Corpus albicans.

Ovogenesis

def.: The process of formation of ♀ gametes. Primordial germ cells [Oogonia] migrate from the endoderm to the ovary of the embryo.

Proliferation: [during 1st trimester of pregnancy]. Oogonia undergo repeated mitosis → large N^o of oogonia (about 7 millions in both ovaries)

Growth: [during 2nd trimester of pregnancy]

Oogonia ↑↑ in size → 1^{ry} Oocytes w enter arrested prophase of 1st meiotic division. By 7th month of pregnancy, many oocytes undergo atresia such that at puberty both ovaries have 300,000 1^{ry} Oocyte

Maturation: At puberty, each month, one 1^{ry} oocyte (2n) complete 1st meiotic division just before ovulation & give 2^{ry} Oocyte (1n) & 1st polar body. After ovulation, 2^{ry} Oocyte enter 2nd meiotic division (completed only after fertilization) → mature ovum & 2nd polar body.

During the fertile period of ♀ (30-40 years), only 450 Ova are produced & Other oocytes undergo atresia.

- **Anti-Müllerian hr. [AMH]:** Formed by small ovarian follicles to regulate their Growth. It's bl. level is an indicator of remaining follicles (ovarian reserve).
- **Polycystic Ovary Syndrome:** most common disorder 5-10% of ♀s. Cause is uncertain (mostly genetic dis.). ♀ shows multiple ovarian cysts. The cysts are 2^{ry} follicles (arrested at early antral stage) & fail to reach mature Oocyte & imbalance in the ♀ sex hrs. leads to irregular menstrual cycle & trouble to get pregnant.

Fallopian Tube [Oviduct]

10-12cm long. Carry the ovum to the uterus. & site of fertilization.

Anatomically, formed of 4 segments:

Intramural segment: pass through the wall of the uterus.

Isthmus: narrow & thick walled.

Ampulla: thin walled & site of fertilization.

Infundibulum: Have fimbria & open into the peritoneal cavity.

Histologically: wall is formed of 3 layers:

1. Mucosa: folded. Formed of:

(a) S. col. partially ciliated epith.: contain:

- Ciliated cells: → push the ovum.
→ at ovulation become taller & more ciliated.
- Secretory cells → watery fluid → nutritive to ova.
→ capacitation of sperms.

(b) Lamina propria of c.t.

2. Musculosa:

Inner circular & out. long. sm. ms. Their peristalsis push the ovum or zygote towards the uterus. [more helpful than cilia].

3. Serosa: = loose c.t covered e' s. sq. mesothelium.

Modifications in the diff. parts of F. tube:

- mucosal folds are most numerous in the ampulla
- Ciliated cells " " " " " infundibulum.
- Secretory " " " " " intramural part.
- Musculosa is thickest in the isthmus & " " " .

Tubal Ectopic pregnancy:

The fertilized ovum occasionally implants in the thin walled Fallopian tube (unsuitable for fertilization). It is perforated as the embryo ↑ in size → bleeding in the peritoneum & severe abdominal pain even shock (in cases & severe bleeding).

Uterus

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Pear shaped organ formed of 3 parts: Fundus, body & cervix. Histologically, fundus & body have the same structure while cervix is different.

I- Fundus & body of Uterus

Formed of 3 layers:

1. Endometrium:

- a. simple col. partially ciliated & partially secretory.
- b. c.t. lamina propria that contains simple tubular gls = endometrial glands lined e' s.col. secretory e' very few ciliated cells.

Functionally, endometrium is divided into:

a-Functional Zone	b-Basal Zone
- the superficial part. - Contains: - Surface epith. + superficial part of lamina propria. + " " " endometrial gls. - Supplied by spiral arteries. - marked changes during the menstrual cycle. - the regenerative part.	- the deep part. - the deep part of lamina propria. • " " " " endom. gls. - Straight arteries. - No changes. - the reserve part.

2. Myometrium:

Very thick, formed of 3 layers: [poorly defined]

- a) Submucosal L. [Stratum Submucosum] = longitudinal sm.ms.
- b) Vascular L. [St. Vasculare] = Circ. & oblique ms → 8-shaped figures around bl.us.
- c) Supravascular L. [St. Supravasculare] = long. sm.ms.

Myometrium is hormone sensitive. During pregnancy it undergoes:

- [hyperplasia (↑↑ N°) & returns to normal (involute) after delivery, in few ws
- [hypertrophy (↑↑ size) After menopause, m.ps atrophy e' ↑↑ fibrous c.t. bet them.

3. Perimetrium: loose c.t. covered e' s.sq. mesothelium.

V.B) The spiral & straight as. arise from the arcuate art. in the myometrium

Fibroids Liomyoma = the most common benign tumor in ♀ = tumor of sm.ms of the myometrium.

II-Cervix of Uterus

The lower cylindrical part (3 cm) protruding into the vagina. Its junction. e' uterus = int. os. & its opening into the vagina = ext. os. Has narrow lumen (1 cm) formed of:

1. Mucosa:

a. Endocervix [cervical canal]:

lined e' s. col. mucus secreting cells + lamina propria containing cervical glands (branched tubuloalveolar mucus secreting) lined e' s. col.

b. Ectocervix: the outer surface & ext. os are lined e' non. Kerat. str. sq.

Cervical mucosa do not show cyclic changes during the menstrual cycle (i.e. do not shed)

2 Stroma:

= dense fibrous c.t. e' few smooth ms., so cervix is firm & rubbery.

During labor, under control of relaxin hr. from the placenta, Cervix becomes soft & dilated due to separation of the parallel collagen bundles w become irregular [collagenolysis].

Collagenolysis: during labor, M concⁿ of hyaluronic A. withdraw H₂O bet. collagen fs. → their separation → cervical dilatation (to reach 10 cm) to pass fetal head

Cervical Mucus:

- plays an imp. role in fertilization.

- During proliferative phase & time of ovulation, cervical mucus is abundant, thin & watery → easy movement of sperms to uterus & fertilize the ovum.

- After ovulation (in secretory phase) or if pregnancy occurs, cervical mucus becomes viscid & scanty to prevent entrance of sperms or bacteria to the uterus.

Smears of cervical epith. are imp. for early diagnosis of cervical Carcinoma

Menstrual Cycle

= Cyclic changes in the endometrium. Starts at puberty [12-15 years] until the age of 45-50 years [= fertile period of ♀]. Under control of FSH & LH of pit. & ovarian hormones [estrogen & progesterone].

Its duration is about 28 days. 3 phases:

1. Menstrual (destructive) phase:

- From 1st to 5th day.

If no fertilization occurs, C.L. stops functioning 10-12 days after ovulation

→ sudden drop of bl. estrogen & progesterone → vasoconstriction of spiral arteries → ischemia & necrosis & shedding of the functional zone

While the basal zone (0.5 mm) remains from w regeneration starts. the capillaries rupture → bleeding

[2] - Proliferative phase : [follicular - estrogenic phase]

- from 5th to 14th day
- under control of pituitary FSH & ovarian estrogen.
- estrogen stimulates proliferation & regeneration of the basal zone (2.5 mm)
- endometrial epith. (s.col. part.cil) regenerates.
- endometrial glands regenerate : become narrow & straight but no secretory function.

[3] Secretory phase : [luteal - progestational phase]

- from 14th day till onset of next bleeding.
 - under control of pit. LH & ovarian progesterone
 - endomet. ↑↑ in thickness (5 mm).
 - endomet. glands : become tall, tortuous, dilated & cells accumulate glycogen in their basal parts, later on glycogen reach the apex of the cells & the lumen of the gland is full of secretion.
 - Spiral arteries : dilated ; tortuous & congested.
 - Stroma : become edematous, fibroblasts ↑ in No & size (rich in ^{mit} GA) & called decidual cells. _{FER}
- These changes are called decidual reaction.

Decidual cells:

1. Secrete prostaglandins: stimulate uterine contractⁿ during labor.
2. " Prolactin : * regulate amniotic fluid vol. & fetal H₂O balance.
* has paracrine control → ↑↑ secretion of the endometrial gls. in 1st trimester.
* affect synthesis of fetal surfactant.
* " Ca⁺⁺ absorption in fetal gut.

The high level of progesterone in " secretory phase inhibits contractⁿ of sm.ms of myometrium not to interfere wth implantation of the embryo

After Fertilization, the embryo reaches the ut. (day 5-6 after ovulation)
its main source of nutrition is the secretion of the endometrial glands.

Placenta

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def. Temporary endocrine gland & the site of exchanges bet. the mother & foetus.

Formed of:

A. Maternal Part = [Decidua Basalis]

the fibroblasts in endometrial c.t. enlarge & show features of ptn. forming cells & now called decidual cells. The thickened endometrium is called decidua.

Decidua is divided into: decidua basalis: bet. embryo & myometrium.

decidua capsularis: bet. the embryo & uterine cavity.

decidua parietalis: endometrium lining the rest of the uterine cavity.

Decidua basalis is the most imp part that forms the placenta.

B. Fetal Part = [Chorioic Villi]

= Finger like projections from the blastocyst. They branch & anastomose & become embedded in the decidua basalis, separated by intervillous spaces containing maternal blood. Each chorionic villus is formed of:

1. Central core of foetal c.t. containing foetal bl. vs & macrophages = Hofbauer Cells

2. Trophoblast: epith. cover: 2 layers:

a. Inner Cytotrophoblast: 1 layer of cuboidal cells & pale cytoplasm

It disappears by the end of 4th month of pregnancy

b. Outer Syncytiotrophoblast: 1 layer of dark cells & no cell boundaries so appear as multinucleated layer. Has microvilli w invade the decidua basalis.

Placental Barrier:

The wall w separates blood in fetal circulation from bl. in maternal circulation.

Formed of:

1. endothelium of foetal capillary.

2. basement memb. of foetal capillary.

3. Foetal c.t. containing Hofbauer cells.

4. Basement memb. of trophoblast.

5. Trophoblast: cytotrophoblast & syncytiotrophoblast in the 1st 4 months (syncytiotrophoblast only in the last 5 months).

Functions of Placenta:

1. passage of O₂, nutrients, hormones, antibodies from mother to fetus.

2. remove CO₂ & waste products.

3. Endocrine function: Syncytiotrophoblast secretes:

a. Human chorionic gonadotropin: maintain corpus luteum of pregnancy after LH of pit. stops.

b. Human chorionic somatomammotropin: lactogenic & growth stimulating

c. Estrogen & progesterone.

d. Chorionic thyrotropin (similar to TSH)

e. " " Corticotropin (" " ACTH).

f. relaxin: softening & dilatation of cervix during labor.

4. placental Barrier functions:

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- protect the embryo from harmful bacteria.
- allow passage of maternal Ig to fetal bl. to passively immunize the fetus against bacteria.

Placenta Previa:

The placenta implants in the lower part of uterus close to the int. os.
The main cause of 3rd trimester bleeding. Usually necessitates emergency Cesarean section.

Vagina

Fibromuscular tube 7-9 cm long. Formed of:

(1) Mucosa:

(a) Non-Keratinized St. sq. epith.:

- estrogen stimulate cells to form & accumulate glycogen.
- As vaginal cells desquamate, glycogen deposit in the lumen.
- glycogen by Vaginal bact. lactic acid → acidic PH to protect against harmful bact. & fungi.
Lactobacilli

(b) Lamina propria: loose c.t. rich in elastic fs.

(2) Musculosa: Inn. circ. & Out. long. sm. ms.

(3) Adventitia: dense c.t. rich in elastic fibres.

The mucus found in the vagina comes from the cervical glands as the vagina has no glands.

The great elasticity of vagina (large N^o of elastic fs in lamina propria & adventitia) allows temporary distention during labor.

The external Genitalia

Labia Majora = 2 folds of fatty skin & sm. ms. The inner surface has no hairs while the outer surface is covered e' hairy skin e' sweat & sebaceous glands.

Labia Minora = 2 folds of skin e' a core of loose c.t. rich in elastic fs. The outer & inner surfaces have sweat & sebaceous gls. but no hairs & no fat.

Clitoris = erectile tissue = 2 corpora cavernosa covered e' thin skin e' no hairs, no sweat or sebaceous glands.

Hymen: perforated memb. at the lower end of vagina = c.t. core covered on both sides by st. sq. epith. = the junction bet. ext. & int. genitalia.

Bartholin's gls: mucous glands on either side of the vestibule

* Vestibulum = the space bet. the 2 labia minora.

Ext. genitalia esp. clitoris are rich in sensory n. endings e.g. Meissner's &

The Mammary Gland

• def. : Exocrine, compound alveolar, apocrine gland.

• Structure & development:

At birth = nipple, surrounding areola + duct system in dense c.t.

After puberty : breast enlarges due to → accumulation of fat
(under control of estrogen) → branching of ducts.

1. In Resting State:

The nipple = raised area of dense c.t. rich in smooth muscles covered e' pigmented skin, rich in sensory ns, & contain opening of 12-20 lactiferous ducts.

Areola : pigmented skin around the nipple e' modified sebaceous glands (Montgomery gls.).

Parenchyma:

12-20 lobes separated by thick c.t. septa rich in fat cells. Each lobe contains branching lactiferous ducts lined e' cuboidal cells, surrounded by myoepith. cells & embedded in abundant loose c.t. Small ducts empty into a large lactiferous duct that dilates → lactiferous sinus (lined e' stratified cuboidal epith.) that changes into str. sq. epith. at it's external opening in the nipple.

2. In Pregnancy & Lactating State:

Under control of estrogen, progesterone, prolactin, chorionic somatomammotropin the following changes occur:

- The breast enlarge in size.
- The nipple & areola become more pigmented (rarely returns to normal color).
- Montgomery gls. enlarge.
- Alveoli proliferate at the end of the ducts.
- Alveoli are lined e' s.col. + myoepith. cells. Col. cells secrete milk, so, rich in mit., rER, G.A. (ptn) + s-ER, fat droplets (lipids).
- Milk is rich in ptns. (1.5%), lipids (4%), lactose (7%) + the apical parts of cytoplasm (apocrine).
- It appears acidophilic & vacuolated due to dissolved fat.
- The C.T. septa become thinner & fat cells ↓↓.
- The amount of loose c.t. ↓↓.

3. Post-lactation changes :

After weaning, most alveoli degenerate & dead cells are removed by macrophages & breast returns to resting state.

4. Post-menopausal changes :

↓↓ estrogen → atrophy & reduced size.

Clostrum = the 1st secretion after labour & less fat, more ptn. & rich in Abs (Ig A) for passive immunity of the newborn.

[Hormonal Control of the breast]:

Estrogen: enlarges the breast at puberty → accumulation of fat & branching of the ducts

Estrogen, progesterone + chorionic somatomammotropin: at pregnancy → enlarged breast & more branching of ducts & development of alveoli.

Prolactin → milk secretion during lactation

Oxytocin → milk ejection by contraction of myoepith. cells

♂ Breast:

= small amount of fibrous c.t. + rudimentary duct system.

It may enlarge at puberty due to accumulation of fat.

This enlargement is mild, self limited & reversible.

Breast Cancer: [in females]

- The first in Egypt & all arabian countries mainly in lactiferous ducts. If malignant cells metastasize to lungs, liver, brain & bone maybe fatal.
- Early detection [by self examination, mammography & ultrasonography] followed by early treatment → better prognosis & ↓↓ mortality.